

### **Remarks**

After entry of the amendment, claims 1-58 are pending.

The specification has amended to correct typographical errors.

Claims 1, 3 and 55 have been amended to comply with the Examiner's restriction requirement for the variable X as Group Xc in the compound of Formula (I).

No issues of new matter should arise and entry of the amendment is respectfully requested.

### **Restriction Requirement**

In response to the Restriction Requirement of September 3, 2004, Applicants elected the elected Examiner's Group X, with traverse. In the Office Action dated December 20, 2004, the Examiner made the restriction requirement final. In view thereof, Applicants are filing concurrently herewith a Petition from Requirement for Restriction Under 37 C.F.R. §1.144.

Applicants respectfully request that the Petition be forwarded to the Group Director for timely consideration.

### **Claim Objection**

Claim 1 has been objected to for typographical errors for the non-elected species.

In view of the amendment to claim 1 to comply with the Examiner's Restriction Requirement and the elected species request of December 30, 2004, the objection is now moot.

### **Response to the Further Restriction Requirement – Election of Species**

In response to the Examiner's further restriction for "X" in the compounds of Formula (I), Applicants elect Examiner's Group Xc, drawn to claims 1-4 wherein X is choice 4, 5, 7-9, 14, 27-28 and 32-33, with traverse.

Applicants thank the Examiner for clarifying the Restriction Requirement dated September 3, 2004.

### **Rejection under 35 U.S.C. §112, First Paragraph**

Claims 1-4 are rejected under 35 USC § 112, first paragraph, as lacking enablement

Applicants respectfully traverse the rejection and respectfully submit that the claims are fully enabled and one skilled in the art could make and use the presently claimed invention without undue experimentation.

MPEP 2164.01(b) states:

As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U. S. C §112 is satisfied. *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970).

MPEP 2164.04 states (emphasis added):

A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U. S.C. 112, first paragraph, **unless there is reason to doubt the objective truth** of the statements contained therein which must be relied on the enabling support.

[I] it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supportive disclosure and **to back up assertions of its own with acceptable evidence or reasoning** which is inconsistent with the contested statement.

The Examiner erroneously states that there is no enabling disclosure by way of working examples or reasonable disclosure leading to the preparation of the compounds of the invention. The specification at, for example, page 62, line 10 to page 121, line 27, has 57 working examples with detailed experimental conditions for the preparation of compounds with numerous structurally diverse linker groups. Additionally the specification at, for example, page 41, line 10 to page 42, line 13, has a description with numerous literature references on how one skilled in the art could synthesis the nitrosated compounds of the invention. Based on the extensive disclosure in the specification and the state of the scientific literature for the synthesis of organic compounds, one skilled in the art would easily be able to prepare any of the compounds disclosed in the specification.

The Examiner also states that “the homogeneity of the 4 examples would provide no insight into structure-activity trends that need to be evaluated. Receptor binding is known to be structure-sensitive in general.”

Applicants respectfully submit that the present invention is not directed to receptor binding. The present application is directed to the composition, kits and methods of use of novel nitrosated nonsteroidal antiinflammatory drugs and dose not involve the receptor binding of the compounds of the invention. Additionally the specification at page 121, line 28 to page 123, line 1, compares the in vivo anti-inflammatory and gastric lesion activity for 29 structurally diverse compounds of the invention. Based on the extensive disclose in the specification one skilled in the art would readily be able to predict the structure-activity relationship of the compounds of the invention.

The Examiner merely provides conclusory statements as to an alleged lack of enablement. If the Examiner maintains the objection, Applicants respectfully request that the Examiner provide evidence why one skilled in the art would not be able to make and use the compounds of the invention as the specification provides numerous detailed working examples.

In view of the above, applications respectfully submit that the claims satisfy the requirements under 35 U. S. C. §112, first paragraph, and respectfully request that the rejections under this provisions be withdrawn.

**Rejection under 35 U.S.C. §112, Second Paragraph**

Claims 1-4 are rejected under 35 USC § 112, second paragraph, as being indefinite.

Applicants respectfully submit that the claims satisfy the requirement under 35 U.S.C. § 112, second paragraph. The response numbers below correspond to the numbers in the Office Action.

1. Applicants respectfully submit that the ACS registry number database is the largest file of substance information in the world containing structures and chemical names of millions of compounds. The database provides information for the structures, names, formulas, properties and ring data for the compounds. These registry numbers are used worldwide in, for example, many public and private databases, governmental regulatory agencies, commercial chemical inventories, and in handbooks, guides and other reference works. Assuming *arguendo* the ACS decided to change and assign new registry numbers to the millions of compounds in its registry number database, in order to prevent total confusion, the ACS would have to provide a means of linking the newly assigned numbers to the old registry numbers. Hence, the ACS registry number will always be a unique number that characterizes a compound.

2. Claim 3 has been amended to comply with the restriction requirement for the choices of the variable “X” for the compounds of Formula (I). In view thereof, the rejection is now moot.

In view of the above, applications respectfully submit that the claims satisfy the requirement under 35 U. S. C. §112, second paragraph, and respectfully request that the rejections under this provision be withdrawn.

### **Examination of Additional Species**

Pursuant to MPEP §803.02, Applicants respectfully request the examination of additional species upon an indication of the allowability of the elected species in claim 1. MPEP §803.02 states that “should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended [to the non-elected species]....The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim.”

The Examiner states that publications WO 02/092072 A2 and WO 03/013499 A2 are devoid of the X linker choice of the elected invention, i.e., Examiner’s Group X for variable Rn in the compounds of Formula (I) in claim 1. These PCT applications disclose nitrosated non-steroidal anti-inflammatory compounds. Hence the Examiner has already searched other nitrosated non-steroidal anti-inflammatory compound directed to the non-elected species of the present invention. Expanding the claims to encompass these and other non-elected species would not be a burden to the Examiner.

Applicants respectfully request rejoinder of the non-elected species of claim 1, wherein Rn is variable 1-10, 13-18 and 20-51.

### **Rejoinder of Claims**

Applicants respectfully request rejoinder of claims 5-54 and 56-58.

The claims in the pending application are generally directed to nitrosated nonsteroidal antiinflammatory compounds, and compositions comprising nitrosated nonsteroidal antiinflammatory compounds, and, optionally, other compounds, kits and the methods of use for the compounds and/or compositions.

If the nitrosated nonsteroidal antiinflammatory compounds of claims 1-4 are allowable, then all the compositions and kits requiring a nitrosated nonsteroidal antiinflammatory compounds would also be allowable and all the methods of use for these compositions would

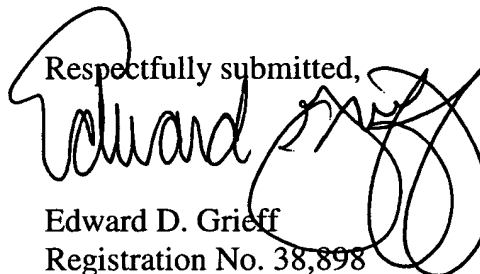
also be allowable. In other words every pending claim that requires a **nitrosated nonsteroidal antiinflammatory compound of claims 1-4** would also be allowable.

Additionally, a search of the prior art for the nitrosated nonsteroidal antiinflammatory compounds of claims 1-4 would necessarily encompass a search of the prior art for the compositions for the nitrosated nonsteroidal antiinflammatory compounds, and, optionally, other compounds of claims 29-39, kits of claims 51-54 and their methods of use of claims 5-28 and 40-50. Thus, the prior art for the nitrosated nonsteroidal antiinflammatory compounds of claims 1-4, will also be the same prior art for the compositions, kits and methods of use for the nitrosated nonsteroidal antiinflammatory compounds of claims 1-4

Applicants respectfully thank the Examiner for his consideration for the rejoinder of of claims 5-54 and 56-58

#### **Conclusion**

An early and favorable reconsideration and allowance of the pending claims is respectfully requested. The Examiner is encouraged to contact the undersigned to expedited prosecution of this application.

Respectfully submitted,  
  
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